Campbell (H. F.)

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CAFFEINE AS AN ANTIDOTE

IN THE

Poisonous Narcotism of Opium.

BY

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CAFFEINE.

It is the design of the present brief communication, to call the attention of the profession to an important, and we think, most valuable application of Caffeine, as illustrated in a case of extreme narcotism from the effects of Opium.

Our knowledge of the vegetable alkaloids, and indeed, of the whole subject of Organic Chemistry, is of comparatively but recent date. In the year 1817, Terturner, a German Apothecary, having announced the existence of Morphia, the spirit of investigation was immediately aroused, and the study of every class of organic bodies has become the favorite occupation of the chemist, and has yielded him a treasury of the most valuable results. This process of investigation is still ardently pursued, and, every day, some new organic compound is being added to the already lengthened list.

"The alkaloids as a class," says Dr. Parrish, "are the most powerful of organic principles, displaying their effects especially on the nervous system, which they so forcibly impress as to constitute, many of them, virulent poisons; a few, however, seem nearly destitute of active properties. They all contain nitrogen, and by destructive distillation, or by treating with alkalies, evolve ammonia; they evince their alkalinity by restoring the color of reddened litmus, and though not always crystalline or even solid, they combine with acids to form definite salts which are crystalline; they also, like the alkalies proper, form double salts with bichloride of platinum."

Most of the alkaloids are said to be but sparingly soluble in water, but they dissolve readily in alcohol, especially with heat. Ether, the essential oils, and chloroform, dissolve most of them, and almost all of them are soluble in benzine. "They are all precipitated from solution, whether alone or combined with salts, by tannic acid, which is hence, when taken immediately, one of the best chemical antidotes for them; they are precipitated by alkalies."*

These principles exist in many plants, but not in a free state, being generally combined with some peculiar vegetable

*See Introduction to Practical Pharmacy, by Edward Parrish. Philad. 1859

acid. "All really poisonous plants are believed to contain an alkaloid or neutral *characteristic principle*, except, perhaps, those few acrid poisons which owe their activity to resins."† To the presence of this neutral principle many of our most valuable remedial agents, especially in the vegetable kingdom, owe all their activity, and by it the phenomena they evoke from the animal economy is characterized.

Whatever may be the peculiar property of the crude vegetable, whether potent for good or for evil, that property is ever found to exist in a higher degree of intensity in its alkaloid representative; hence, of late years, since these principles are becoming better known to the Medical Profession, many of them have entirely displaced as remedial agents, their more bulky sources on account of their far greater potency and unmixed action. Thus quinia and its salts have entirely replaced, as an antiperiodic, the weaker and more bulky Peruvian bark, while the salts of morphia are rapidly supplying the place of all the other preparations of opium, and, except for the intensity of their action, strychnine and atropine would long ago have driven all the other preparations of nux vomica and of belladonna, out of the catalogue of remedial agents.

For a long period it has been well known to the profession, and even in domestic life, that coffee, *Coffea Arabica*, possessed virtues as a stimulant of a most valuable, and at the same time, of a peculiar kind. In the London Medical Times & Gazette, of June, 1855, Dr. Julius Lehman has shown that coffee is powerful as a stimulant in increasing the nervous energy, and that it also retards the metamorphosis of the tissues. It is further considered that one of the physiological effects of coffee is to lessen the elimination of urea. Prominent among the alleged effects of coffee is its *antisoporific* power, or that of inducing *wakefulness* when taken in large quantities, or by persons unaccustomed to its use. With this effect every one is familiar who has ever indulged in this common beverage.

The therapeutic applications of coffee in the form of infusion or decoction, have been various and long known to the Profession. It has been highly recommended as a remedy in Cholera Infantum*; it is said to quiet nausea in many cases of irritable stomach, a fact which we have ourself verified; its

‡Ibid.
*Dr. Pickford. London Medical Gazette, Nov. 24, 1848.
†See Materia Medica and Therapeutics, by T. D. Mitchell, M. D., &c.

use is prophylactic as well as curative in intermittent fever—it has long been a valued remedy with some asthmatics—is said to be one of the best agents for overcoming the effects of alcoholic liquors—has been, from time immemorial, the favorite beverage of opium-eaters, and is frequently administered to counteract the effects of this and other narcotic poisons. The use of coffee for this purpose was common some forty years ago in this country, and several of the theses of the University of Pennsylvania, on the subject, were printed. Very strong *decoctions*, without sugar or milk, were recommended for this purpose. All opium-eaters are said to be great coffee-drinkers. Beaujour, in his work on Greece, gives an account of an opium-eater who drank "more than sixty cups of coffee a day, and smoked as many pipes. All this was designed to counteract the pernicious action of the opium."†

In the Edinburgh Medical & Surgical Journal for January, 1842, a case of poisoning is reported, caused by one and a quarter grain of sulphate of morphia, equal to seven and a half grains of opium. The cure was effected by gill doses of strong decoction of coffee frequently administered. Were it necessary, we could easily adduce many more witnesses of the therapeutic application of coffee, but the above is sufficient to show that it has been long known as a powerful agent in many diseases, and further, that it has been fully recognized as a valuable means of counteracting the effects of opium. We have for years been in the habit of giving strong doses of the decoction of coffee in cases of over-doses of opium, and have seldom treated a case without applying it—after other and more efficient remedies, as the stomach-pump, emetics, &c., have emptied the stomach—to re-animate the patient and to overcome drowsiness.

As we have just said, whatever may be the peculiar medical or physiological action of any vegetable medicinal agent, its alkaloid representative has been generally found to exercise that influence in a far more efficient manner than the crude source from which it was obtained. This is thought to be eminently the case, with regard to *Caffeine*, the alkaloid active-principle of coffee.

There are several vegetable alkaloids which are said to be identical with Caffeine, both in their chemical constitution and in their effects on the animal economy. Theine obtained from Tea, and Guaranin, from the Guarana—Paullina Sorbilis*—

*According to Von Martius, an extract is prepared in Brazil from Paullina

are each said to possess virtues which, in no respect, vary in their effects from that of Caffeine.

"Caffeine is procured by exhausting bruised *coffee* by two successive portions of *boiling water*, uniting the infusions; adding acetate of lead to precipitate the principles which accompany the caffein; filtering and decomposing the excess of acetate of lead in a filtered liquor, by sulphuretted hydrogen; concentrating by evaporation and neutralizing with ammonia. The Caffein is deposited in crystals, upon cooling, and may be purified by re-dissolving in water, treating with animal charcoal and evaporating."† It presents itself in the form of long, silky needles; is fusible, volatile and soluble in water, alcohol and ether.

Phobus is inclined to doubt "whether caffeine is of the importance that has been assigned to it; but Von Falck, from much observation, ascribes to it a highly powerful and even poisonous action. Experiments on the lower animals have been made with caffeine by several physiologists; Albers of Bonn, produced tetanic phenomena by its administration to a frog, and the same symptoms were induced by inserting a solution of the citrate of caffeine under the skin of the thigh of another frog." Mulder gave a grain of caffeine to a rabbit; the animal ate but little the next day, and aborted the day after. Lehman gave it in doses of from two to ten grains, and reports§ that, "it caused violent excitement of the vascular and nervous systems, palpitations of the heart, extraordinary frequency, irregularity, and often, intermission of the pulse; oppression of the chest, pains in the head, confusion of the senses, tinnitus aurium, scintillations before the eyes, sleeplessness, erections and delirium; and, in all cases, there was an increase in the amount of urea secreted." It is extolled by Hannon and Eulenberg in the various forms of Hemicrania, and has been frequently used for the same purpose, by the practitioners both of England and of this country. Of the application of caffeine as an antidote in the poisonous narcotism of opium, we have as yet seen no published account, and hence we have deemed the subject of sufficient importance to call the attention of the profession to the details of the following case:

Sorbilis, which is known there under the name of "Guarana," which is employed successfully in chlorosis, tedious convalescence, paralysis, the colliquative diarrhœa of Phthisis, and in hemicrania.

See Dunglison's New Remedies, p. 573.

†Dispensatory of the United States, 10th ed., p. 1318.

§Physiological Chemistry.

Extreme Narcotism of Opium promptly relieved by Artificial Respiration and the administration of Caffeine, by Injection.

Monday, Oct. 10th, 1859, 8 o'clock, P. M.—We are called in haste to Mr. F. H. T., aged 24 years, who, it was said, had taken laudanum, and was in imminent danger from the effects of the drug. We found the patient in the clerk's office of one of the hotels of this city. He was lying on a sofa with his head supported in the lap of a friend. His respiration was very slow, though not counted at the time—pulse full, but of nearly normal frequency—he was completely insensible—tongue and lips purple, and muscular system greatly relaxed. It was positively known that he had taken, in a fit of temporary depression, over *one ounce and a half of laudanum*, nearly an hour before the time of the present visit.

The condition of the patient was so alarming that we *began the treatment* by the pouring of cold water on the head till the stomach-pump could be applied—for on attempting to introduce the tube into the œsophagus, respiration appeared to cease altogether—the entire muscular system was so completely relaxed that the tongue hung out of his mouth, and was pushed about by the end of the stomach-tube, in certain positions, folding back into the fauces, and apparently obstructing respiration. The attempt to use *emetics* was of course out of the question. The continued use of ice-water upon the head, and the occasional resort to artificial respiration, in a short time improved his condition a little—a very little—and we were willing to introduce the stomach-tube. This was effectually applied; large quantities of tepid water being repeatedly introduced into the stomach and again pumped out. Laudanum was detected both by its odor and color in the fluid first discharged from the stomach. At the end of an hour, his condition becoming apparently more urgent than before the use of the stomach-pump, he was taken from the clerk's office to a room on the second floor of the hotel, where he was undressed and placed in bed, and the application of ice-water to the head was resumed.

12 o'clock, midnight.—The condition of the patient was now decidedly worse than it had been at any previous time; the surface was cold, and purplish from imperfect aeration of the blood, the muscular system, if possible, more relaxed than ever, the respiration, fearfully slow, when counted, by the watch, was found to be *but four to the minute*. The intervals

between the inspirations were now irregular, and each time we had to resort to shaking and slapping the patient to provoke the automatic action of the respiratory muscles, and to raising him up suddenly to the sitting posture, with the same object. The tongue had to be constantly pressed forward with the fingers to prevent its falling back and obstructing the opening of the glottis. The imperfect and irregular action of the heart became now more alarming than ever. It was found that, in the reclining position, this symptom of the case was more alarming than when the patient was placed in the sitting posture. Several times the intervals between the beats of the pulse led us to fear that the patient had expired, but on elevating him, the action of the heart became more regular. He was now kept in the elevated position, and not allowed to recline except for a moment at a time, for fear that he would die immediately. Ceaseless efforts were now necessary on the part of his attendants to provoke the respiratory movements. Surrounded by his friends, several of whom were remarkably self-possessed and indefatigable, not a moment was allowed to pass without some effort, as by shaking, compressing the chest, &c., to excite inspirations. No time was now to be lost—but our best efforts at exciting respiration began now to fail to have any effect, and it was evident that *artificial respiration* was now, the only possible hope for the patient. This measure, under the circumstances, was a natural suggestion, but for reasons sufficiently apparent, it seemed impossible to carry it out in the present case; most of the ordinary means of effecting artificial respiration seemed to us impracticable, on account of the delay involved in their performance, and Dr. Marshall Hall's "Ready Method" involved the horizontal position, in which situation, it was clear to the minds of all present, the patient would die immediately.

Artificial Respiration in the Sitting Posture.

1 o'clock.—Under these circumstances, we devised a method of artificial respiration which was well adapted to the condition of the patient—indeed, the only one possible—and which we do not recollect to have seen reported any where in the writings of any one on this subject.

The patient was supported in the sitting posture, by an assistant kneeling on the bed at his back and holding his head erect between his hands; two other assistants standing on each side of the patient now took charge of an arm each, holding he limb firmly at the elbow and upper part of the forearm;

the tongue was now pressed down by the handle of a spoon, or the fingers introduced into the mouth; *the assistants having charge of the arms, were now directed to elevate these limbs simultaneouslg, carrying them above the head at an angle of about forty-five degrees, and dragging upon them so as to slightly lift the patient; the arms were then depressed and brought down close against the sides of the Thorax so as to compress the chest.*

The effect of these movements was the following: At each attempt at lifting the body by the arms in this way, forcible *traction outwards* was made on the walls of the chest, through the pectorales major and minor muscles, the serrati and parts of the two latissimi dorsi muscles—giving rise to expansion of the walls of the thorax; the air was thus caused to enter forcibly into the lungs, and thus *inspiration* was completed. The arms were then brought steadily down, and pressed against the sides of the thorax and abdomen—compressing them and expelling the air forcibly from the lungs and effecting *expiration.**

Under the use of the artificial respiration, the appearance of the patient was much improved. The color was restored to the face, the lips became redder, and the countenance more natural, though the relaxation of the muscular system was by no means lessened; if the head was left unsupported for an instant, it fell forward as suddenly and forcibly as that of a dead man. The artificial movements were continued for more than an hour, and though the color of the patient was improved and the heart's action became normal, still when they were omitted, there was found no improvement in the natural respiration, these being still, *but four times in a minute*, as before artificial respiration was applied.

We now felt the necessity of adopting some means of introducing a stimulant or anti-narcotic agent into the system. *Strong Coffee* naturally presented itself to our mind, but the only preparation we could obtain at that time, was a rather weak infusion left from the supper at the hotel. It was clearly impossible for the patient to *swallow* anything, and we did not think it advisable to run the risk of introducing the stomach-tube in his present condition; we therefore called for a syringe, but the weakness of the coffee caused us to hesitate about using it, when, fortunately, the idea of *Caffeine* occurred

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*A more extended description of this "Natural method of Artificial Respiration" will be given hereafter.

to us, and we sent immediately for that preparation. The artificial respiration was then energetically resumed, in order to prepare the patient for being placed in the horizontal position. A small quantity of the Caffeine was rubbed upon the tongue and to the inner surface of each cheek. The patient was then laid upon his side, *and an injection of the coffee with a large quantity* (*afterwards ascertained to be* TWENTY GRAINS) *of the Caffeine dissolved in it, was administrred by the rectum*, with a common syringe. The patient was then immediately raised again to the sitting posture, and the artificial respiration resumed.

In less than *half an hour*, we perceived that occasionally, between the artificial movements, the patient would effect a *natural inspiration*—these became more frequent, and soon rose to about eight in the minute. He was then laid down and the artificial respiration omitted. The assistants, however, were directed still to remain on the bed and to retain their hold on his arms, that they might resume their efforts at any moment. An hour had not elapsed from the administration of the injection, when the patient, to the astonishment of all present, *forcibly jerked his left arm from the assistant!* (which was the first action of the voluntary muscles he had performed) and immediately began to twist himself in bed, and told those about him, angrily, "to let him alone!"

From this time, he did not again sink into the comatose state, and the relaxation of the muscular system did not return. The respiration became more and more natural, but he remained drowsy, and efforts were continued occasionally to prevent his remaining too long asleep.

The condition of the patient during the remainder of the night, (from 2 o'clock till daylight) was very peculiar; his eyes were heavy, he seemed greatly inclined to sleep, and occasionally would snore a little, but yet he appeared quite cognizant of everything going on around him, and of all the remarks made by his attendants; he had great repugnance to being held or touched. During the earlier part of the narcotism, one of his friends, a young man, tried the expedient of tickling him on the ribs and lower part of the abdomen, with the hope of arousing him; then, the tickling had no effect whatever, but now, it seemed to produce the most painful annoyance, and vexed him beyond all control. The measure was advised, nevertheless, to keep him from falling asleep. He would lay apparently asleep, but before the hand could

reach the surface, he seemed to be aware of the intention, and would select the offender from the whole crowd of his attendants, and aim the most angry blows at him with great accuracy; and, finally, on one occasion, before he could be restrained, he jumped out of bed and followed him to the head of the steps, threatening to shoot him if he thus annoyed him again.*

We left him at daylight. His drowsiness at that time was not very marked.

11th.—We called at the hotel at 10 o'clock, A. M., to see Mr. T., and were informed that he had "gone home to his own residence, nearly a mile distant, at the lower part of the city."

12 o'clock, M.—We were called in haste to see our patient. Found him in a most excited condition; he seemed somewhat alarmed, his face was flushed, his eyes presenting an unusual brightness; he complained of head-ache, great restlessness, and the surface was covered with a profuse perspiration; the pulse was full, quick and frequent. He stated that he had had an alarming attack of a nervous character, which he referred to irregularity and palpitation in the action of the heart.* This had subsided, however, after taking a stimulant, and his condition was such as just described. Prescribed the application of cold water to the head, and that he remain quiet at home till his excitement had subsided. He rapidly recovered and was well in a few days.

There is but a single additional remark which we would desire to make on the effect of Caffeine, as observed in the foregoing case. Mulder, as we have seen, gave this alkaloid to rabbits, and the animals aborted on the second day after its administration; Albers, in one series of experiments on frogs, administered the agent by the stomach, and in another, introduced it into the tissues beneath the cutaneous surface—the effect in both instances, was to produce a *tetanic condition of*

We have been thus minute in the description of these latter manifestations because this peculiar sensibility and irritability appeared to us to be the result of the *Caffeine*, and we think it important to relate *every thing* which evidenced its influence on the nervous system, when administered in such a large dose. The irritability was not the ordinary *itching of the skin* following opium; (he had that too) but an intolerance of all impressions made on the surface, accompanied with a singular *watchfulness* of the mind, (considering his tendency to sleep) on certain subjects. He never, for a moment, seemed to forget that he was in danger of being tickled, and on no occasion did he mistake any other necessary handling of his person for an attempt to annoy him. There was a clearness of the mind in this respect, which was truly remarkable.

*We would here state that we would not advise the administration of the Caffeine in such large quantity, viz: xx grains, as we used in the above case. Did the occasion occur again, we should use *repeated* doses of v or x grains, till the desired effect was produced.

the muscular system. In our patient, *the muscular relaxation was extreme;* his head would fall from side to side, his tongue hung out of his mouth, in the prone position, and fell back into the fauces, in the recumbent posture; not a fibre in his entire muscular system seeming to possess its normal tonicity. And yet, in less than an hour after the administration of a very large portion of Caffeine by the rectum, all this had suddenly disappeared, and he was in the exercise of the most active muscularity; pulling away from his attendants, pushing them from his bed-side, jumping out of bed, and performing every variety of movements in the most energetic and well co-ordinated manner. From this simple collocation of the experimental facts of Mulder and Albers, and of the observed facts presented by our case, there certainly appears to be *a relation* between the phenomena of the one and those of the other which has a bearing on the *muscular system.* Caffeine, it would appear, then, somewhat in the same manner as strychnine, may be regarded as one of our most efficient agents for *restoring muscular contractility*, and for reviving the *tonicity* of the muscular fibre.

The principal object of the present report, however, is only to extend the results of the above remarkable case, wherein the *antinarcotic* effect of the drug had been very apparent; and we therefore desire to dwell no longer on incidental physiological phenomena. If in Caffeine, so powerful an alkaloid—possessing, in a concentrated form, all the antisoporific virtues of Coffee—we have thus found an *antidote* for the narcotic effects of opium, and one which can be applied even in the most extreme states, *by injection*, we must feel that an important extension of its application as a therapeutic agent, has been made, and that many lives may be saved hereafter, by its use. Reasoning from the result of a single case, it is true, however remarkable that case may be, is, we are aware, always more or less unreliable; but, with the most jealous interpretation of the phenomena, as we observed them, we have been forced to the belief that the means used here, acted most powerfully, in producing the favorable result. Indeed, we have never witnessed sequences after the administration of a medicinal agent, which impressed us more fully with the conviction of *cause and effect.* We would, however, take occasion, in closing, to urge the repetition of the administration of Caffeine in cases of Opium-Coma, to a sufficient number of the many which are daily occurring under the eyes of the Profession, in order to prove or disprove the validity of our confidence in the remedy